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Journal Club Review of Diabetic Foot Infections

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Abstract

The general purpose of this journal club is to review foundational articles in the diagnostic and surgical treatment of diabetic foot infections and osteomyelitis. These articles help form the basis for clinical decision making and best treatment practices involving outpatient and inpatient care for diabetic foot infections.

Keywords

Diabetic Foot Infections

Conflict of Interest Statement

None of the authors have conflicts to disclose

REVIEW

Journal Club Review of Diabetic Foot Infections

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Abstract

The general purpose of this journal club is to review foundational articles in the diagnostic and surgical treatment of diabetic foot infections and osteomyelitis. These articles help form the basis for clinical decision making and best treatment practices involving outpatient and inpatient care for diabetic foot infections.

Keywords: Diabetic foot infections

1. Introduction

Diabetes, diabetic foot infections, and subsequent minor and major lower extremity amputations increase the 3 and 5 year mortality rates for patients. A pedal ulcer increases the three year mortality rate for a patient with diabetes from 13% to 28% and patients who receive a lower extremity amputation have a five year mortality rate of 60%.[1] Diabetes, and the complication of diabetic polyneuropathy, increases the risk for pedal wound formation which creates a portal for infection. Infections, though often a simple cellulitis, can be as serious as gangrene with subcutaneous emphysema. Treatments include oral and IV antibiotics, wound debridement, incision and drainage, antibiotic beads, and minor and major amputations. Evaluation, diagnosis, and treatment of diabetic wounds and infections should be performed efficiently and accurately in order to give the patient the best chance for avoiding major and minor amputations; effectively lengthening their lives and increasing their quality of life. Each diabetic foot infection benefits from a team approach to care. The primary physician, podiatrist, vascular surgeon, infectious disease specialist, endocrinologist, and pharmacist are all essential parts of this team who can, together, diagnose the condition, monitor its progress, and provide the pharmaceutical and surgical interventions that maximize the chance for complete healing.[1]

We present to you a few journal articles that focus on the evaluation and treatment of the diabetic foot in cases of infection and concurrent osteomyelitis. The four journal articles presented herein are:

Study A: Probing to Bone in Infected Pedal Ulcers
Study B: Osteomyelitis: Approach to Diagnosis and Treatment
Study C: Diagnostic and Prognostic Value of Erythrocyte Sedimentation Rate in the Contiguous Osteomyelitis of the Foot and Ankle
Study D: Leukocytosis is a Poor Indicator of Acute Osteomyelitis of the Foot in Diabetes Mellitus

2. Study A

Grayson ML, Gibbons GW, Balogh K, Levin E, Karchmer AW. Probing to bone in infected pedal ulcers. A clinical sign of underlying osteomyelitis in diabetic patients. *JAMA*. 1995; 273(9):721−723.

This was a Level III study designed to assess the diagnostic technique of probing to bone in diabetic ulcers to determine the presence of osteomyelitis. This was a prospective study performed from 1988 to 1990 on 76 patients with 77 infected pedal ulcers prior to debridement. Exclusion criteria included patients without pedal ulcers and those with non-healed surgical wounds or infected pedal wounds that had been debrided in such a way that exposed bone. A sterile, blunt 14.0 cm 5F stainless steel eye

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probe was used to probe the wounds at bedside and the exam was considered positive if the examiner palpated rock hard, often gritty, base to the wound without overlying soft tissue. A negative result was recorded if this was not the case. Osteomyelitis was confirmed by surgical pathology after bone biopsy or, in cases where bone biopsy was not obtained, by radiographic evidence of osteomyelitis.

Contiguous osteomyelitis was diagnosed in 66% of the infected pedal ulcers. Of those wounds with confirmed osteomyelitis, 66% of those wounds had a positive probe to bone test and 34% did not. Of the 26 ulcers that did not have osteomyelitis present, only four had a positive probe to bone test. Thus the probe to bone test had a sensitivity of 66%, a specificity of 85%, a positive predictive value of 89%, and a negative predictive value of 56%.

Limitations include a non-randomized trial design and the fact that not all the cases of osteomyelitis were confirmed with the gold standard of surgical pathology.

The authors conclude that this study shows that a probe to bone test of infected diabetic wounds is an effective and useful diagnostic tool that is quick, easy to perform, and cost effective. They suggest that "probing to bone be incorporated into the routine initial assessment of diabetic patients with infected pedal ulcers".[2]

This article introduced a powerful diagnostic tool for evaluation of contiguous osteomyelitis in the presence of infected diabetic wounds that has little cost. It changed the way diabetic wounds were evaluated to the benefit of millions of patients.

3. Study B

Fritz JM, McDonald JR. Osteomyelitis: approach to diagnosis and treatment. *Phys Sportsmed*. 2008; 36(1):nihpa116823. https://doi.org/10.3810/psm.2008.12.11.[3]

This is a diagnostic study with an attempt to help the reader understand the many factors that are to be considered when dealing with osteomyelitis (OM). The author's purpose is stated as; "The approach to osteomyelitis should be guided by several principles, but must be individualized to each unique situation." The pathology involved is multifaceted and each patient has varying complications that a "one size fits all" approach is insufficient.

The three categories of OM most dealt with in medicine include; hematogenous osteomyelitis, contiguous focus without vascular insufficiency from trauma our direct inoculation from a chronic wound, and then there is contiguous infection with vascular insufficiency that is almost exclusive to the lower extremities.

The pathogenesis of OM reminds the reader to consider the virulence factor of the bacteria present, the biofilm, host response to combat the infection can also damage bone, and the increase in pressure can also tip the equilibrium causing bone necrosis.

The signs and symptoms of hematogenous OM likely to occur in the vertebrae and long bones of younger patients. For OM with a contiguous focus, the presentation is likely to include pain, fever, purulence. The OM with vascular insufficiency is frequently present in the small bones of the feet. Likely to present without pain due to neuropathy and impaired vasculature.

A clinical exam is important. Grayson's classic article "Probe to Bone" identified the importance of exploring the underlying structures with a sterile probe.[2] In this study, a positive predictive value of the bone being visible or detected by a probe was 89% correlated with the pathology reports diagnosing OM. Imaging of x-rays and MRI coupled with blood cultures, bone biopsy with histopathology and tissue culture are building blocks for a treatment plan.

Each of the three categories of OM have their most common pathogens. The hematogenous OM is likely to be monomicrobial, OM with and without vascular insufficiency is typically polymicrobial but for different reasons. For OM without vascular insufficiency, S. Aureus is most likely included. OM in the setting of vascular insufficiency also is likely to contain S. Aureus, Streptococci, Gram negative. Pseudomonas is less likely but still an option.

Empirical antibiotic therapy for OM should consider the most likely offending agents but with appropriate antibiotic stewardship. There is growing support from recent literature than oral antibiotics are just as effective at IV. Two recent studies that support antibiotic stewardship is the New England Journal of Medicine 2019 publication of Oral versus IV antibiotics (OVIVA trails) and Oral Is the New IV. Challenging Decades of Blood and Bone Infection Dogma: A Systematic Review from Wald-Dickler et al. in The American Journal of Medicine, 2021.[4,5] These two articles should be considered in our treatment algorithm for therapy.

Surgical management is considered the cornerstone or most definitive treatment of source control for OM. When this is not an appropriate option, selection of antibiotics with high bioavailability, and good bone penetration with effective susceptibility to the bacteria should weigh heavily in our decisions as we care for the patient.

4. Study C

Rabjohn L, Roberts K, Troiano M, Schoenhaus H. Diagnostic and prognostic value of erythrocyte sedimentation rate in contiguous osteomyelitis of the foot and ankle. *J Foot Ankle Surg*. 2007; 46(4):230–237. https://doi.org/10.1053/j.jfas.2007.03.004.

This was a level II prospective study with the purpose of "evaluating diagnostic and prognostic efficacy of erythrocyte sedimentation rate (ESR) for contiguous pedal osteomyelitis (OM)."[6]

The inclusion criteria for this paper included patients who were admitted to The Graduate Hospital from July 2004 to July 2005. Patients were included if they had "suspected OM involving bone distal to the tibiofibular syndesmosis but including the lateral and medial malleolus. Patients with the following comorbidities were excluded from the study: Rheumatoid arthritis, cancer with or without malignancy, polymyalgia rheumatica, sepsis suspected from source other than lower extremity infection, temporal arthritis, multiple myeloma, and steroid use. The criteria used found 95 patients were included in the study. Upon admission, each patient was put on broad-spectrum intravenous antibiotics. ESR values were taken within 48 hours of before bone pathology specimens were taken. After pathology confirmed osteomyelitis in 16 patients; 8 patients that were confirmed to not have OM after long term treatment were compared with 8 patients that were confirmed to still have OM despite long term treatment. The ESR of these patients were taken intermittently over at least 56 days to see trends based off the patient healing or not healing. The data was evaluated using "unpaired, 2-tailed Student *t* tests." The data was plotted with graphs and trends were found using "computerized dPlot programming (Hyde Soft Computing, LLC, Vicksburg, MS)."

Of the 95 patients, 44 were women and 51 were men. 74 had diabetes and 21 did not. 66 patients had acute or chronic OM. After evaluating and averaging the ESR of different patients they found the following. The average ESR for a patient with OM was 76.2 mm/h with a 35.7 standard deviation compared to 59.2 mm/h with a 24.7 standard deviation in those without OM. They future categorized average ESR with patients with diabetes and without. The group of DM patients with OM had an average ESR of 77.4 mm/h while DM without OM had a 62.6 mm/h. The OM patients without DM were found to have an average ESR of 72.3 mm/h and those without OM and DM were found to have an average of 50.4 mm/h. In addition to comparing ESR averages, the group of 16 whose ESR levels were tracked over a long period were evaluated for trends. In the first group that later tested negative for OM after treatment were found to have ESR levels that continued to decrease over time. In the group that tested positive despite long term treatment it was found that in 6 out of 8 patients the ESR level trended upward while one patient was only followed for 35 days was found to have up-trending ESR levels as well. Finally, one patient with confirmed OM after long term treatment was found to have down-trending ESR levels. Using their data, they were able to also calculate positive predictive value (PPV) and negative predictive value (NPV) for ESR and contiguous OM. They found that an ESR of 70 mm/h was found to have a PPV of 82.6% and a NPV of 65.5%. An ESR of 65 mm/h was found to have a PPV of 80.0% and a NPV of 58.6%. Finally, an ESR of 60 was found to have a PPV of 77.0% and a NPV of 55.1%.

The authors conclude that, "ESR can be used in a diagnostic capacity to evaluate a patient for the presence of OM in the foot caused by a contiguous source."[6] This conclusion was supported by their data as it showed significant differences in average ESR in patients with OM versus those without OM. The evidence is stronger because of their exclusion criteria which excluded patients who had comorbidities that would also cause an increase in ESR levels. They also evaluated the difference between OM with and without DM which further helps illustrate its effectiveness. These results show that ESR is an important tool to use when evaluating suspected OM in abscesses, ulcerations, open fractures, bites, and puncture wounds.

5. Study D

Armstrong DG, Lavery LA, Sariaya M, Ashry H. Leukocytosis is a poor indicator of acute osteomyelitis of the foot in diabetes mellitus. *J Foot Ankle Surg*. 1996; 35(4):280–283. https://doi.org/10.1016/s1067-2516(9680075-5).[7]

This was a level II retrospective study with the purpose of establishing leukocytosis as a primary indicator of acute osteomyelitis of the foot in diabetes mellitus.

The inclusion criteria for this paper included type 2 diabetic patients admitted to the University Hospital in San Antonio, TX between January 1, 1990 and December 30, 1992 with acute osteomyelitis secondary to neuropathic ulceration. Patients that were excluded from this study were patients that did not have an erythrocyte sedimentation rate or white blood cell count drawn on admission. The

authors retrospectively reviewed the records of 36 patients with only 28 of those records being included in this study. All subjects were diagnosed with diabetes mellitus using World Health Organization criteria. All subjects had loss of protective threshold diagnosed with the Semmes Weinstein monofilament wire system. A diagnosis of osteomyelitis was based on intra-operative bone cultures at the time of admission and or histologic evidence of osteomyelitis. All patients presenting for care were diagnosed with acute osteomyelitis secondary to neuropathic ulceration. Ulcers were present on average for 81.1−81.7 days. Patients showed signs of infection for 7.2−13.1 days before seeking medical care. Lab values and oral temperature were collected at the time of admission.

Leukocytosis at the time of hospital admission was present in only 46% of patients. 18% of patients had hyperpyrexia. 96% of patients had abnormal erythrocyte sedimentation rate (>20 mm/hr). The results of this study indicate that white count and oral temperature are relatively poor indicators of the presence of infectious disease and diabetic patients. 54% of patients presenting with foot osteomyelitis had normal WBC counts. 82% of patients had a normal oral temperature.

The authors conclude that both WBC count and erythrocyte sedimentation rate are helpful indices to evaluate osteomyelitis, but they need to be used in the context of the entire clinical picture. They state that although elevated laboratory values should alert the clinician to the possibility of sepsis, values that fall within normal limits should not be used as the primary criteria to rule out infection or grade severity of infection.

Declaration of competing interest

None of the authors have conflicts to disclose.

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